

## Advantages and disadvantages of FDA-approved HIV immunoassays used for screening by test format and CLIA complexity<sup>1^</sup>

HIV immunoassays	Advantages	Disadvantages
<b>p24 Antigen (Ag)/IgM/IgG antibody sensitive assays recommended for laboratory-based screening*</b>		
<b>Abbott Architect HIV Ag/Ab Combo Assay</b>  <b>Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV) Assay</b>  <i>Both are fully automated CLIA-moderate complexity HIV tests</i>	1) Highly sensitive during early HIV infection 2) Requires minimal technician time to process specimens 3) Quality control is run once daily 4) Automated platform used for testing is capable of running tests for comorbid pathogens	1) Requires specialized equipment and trained technicians to conduct testing 2) Does not differentiate the p24 antigen from the HIV-1/2 antibody results 3) The ADVIA currently is only approved for serum specimens.
<b>Bio-Rad 2200 HIV Ag-Ab</b> <i>CLIA-moderate complexity fully automated HIV test</i>	1) Detects and reports separate results for: <ul style="list-style-type: none"> <li>• HIV-1 p24 Ag</li> <li>• HIV-1 Ab (groups M &amp; O)</li> <li>• HIV-2 Ab</li> </ul> 2) Highly sensitive during early HIV infection 3) Requires minimal technician time to process specimens 4) Quality control is run once daily	1) Requires specialized equipment and trained technicians to conduct testing
<b>Bio-Rad GS HIV Combo Ag/Ab EIA</b>  <i>CLIA-high complexity. Intended for manual use and with the Bio-Rad EVOLIS™ Automated Microplate System (semi-automated)</i>	1) Highly sensitive during early infection detection 2) Quality Control is included in each run 3) In low volume testing situations, there is the option to run manually using more compact and less costly EIA plate washers and readers.	1) More labor intensive than fully automated platforms 2) Requires specialized equipment and trained technicians to conduct testing 3) Does not differentiate the p24 antigen from the HIV-1/2 antibody results 4) Long turnaround time (> 3 hours); if delivery of test result is delayed there is an increased likelihood person tested may not receive results
<b>p24 Ag/IgM/IgG antibody sensitive rapid lateral flow immunoassay*#</b>		
<b>Alere Determine HIV-1/2 Ag/Ab Combo</b>  <i>CLIA-Waived when used with whole blood</i>	1) More sensitive for early HIV infection than all rapid antibody only HIV tests 2) If test is performed at point of care, high likelihood that person will receive test result	1) Not as sensitive for early HIV infection as p24 Ag/IgM/IgG sensitive HIV tests.

<b>IgM/IgG antibody sensitive laboratory-based assays~</b>		
<b>ADVIA Centaur HIV 1/O/2 Enhanced (EHIV)</b>  <i>CLIA-moderate complexity fully automated</i>  <b>Ortho Vitros ECI/ECiQ Anti-HIV 1+2</b>  <i>CLIA-high complexity fully automated</i>	1) Turnaround time for initial result is < 1 hour 2) Requires minimal technician time to process specimens 3) More sensitive for early infection than rapid antibody HIV tests and IgG sensitive tests 4) Ortho (per product insert): only borderline reactive specimens need to be repeated, and quality control is run once daily	1) ADVIA (per product insert): specimens must be bracketed with quality controls 2) Not as sensitive for early infection as p24 Ag/IgM/IgG sensitive tests 3) Requires specialized equipment and trained technicians to conduct testing
<b>Bio-Rad GS HIV-1/2 Plus O</b>  <i>CLIA-high complexity manual or semi-automated HIV immunoassay</i>	1) More sensitive for early infection than rapid antibody HIV tests and IgG sensitive tests 2) In low volume testing situations, there is the option to run manually using more compact and less costly EIA plate washers and readers	1) More labor intensive than fully automated platforms 2) Not as sensitive for early HIV infection as p24 Ag/IgM/IgG sensitive tests 3) Long turnaround time (> 3 hours); if delivery of test result is delayed there is an increased likelihood person tested may not receive results
<b>IgM/IgG antibody sensitive flow-through rapid HIV immunoassays~++</b>		
<b>INSTI HIV-1/HIV-2 Antibody Test</b>  <i>CLIA-waived when used with whole blood. Moderate complexity when used with serum or plasma</i>	1) Test is shown to detect HIV gp41 specific IgM antibodies in early HIV infection which enhances its utility in early HIV infection <sup>1</sup> 2) Quick turnaround time (< 5 minutes) 3) Test can be read immediately after adding reagents. 4) Portable 5) If test is performed at point of care, high likelihood that person will receive test result	1) Less sensitive than IgM/IgG and p24 Ag/IgM/IgG sensitive laboratory-based tests
<b>IgM/IgG antibody sensitive Rapid Lateral Flow immunoassay#~</b>		
<b>Uni-Gold Recombigen HIV-1/HIV-2</b>  <i>CLIA-Waived when used with whole blood. Moderate complexity when used with whole blood</i>	1) CLIA-waived tests can be performed by non-laboratorians 2) Quick turnaround time (20 minutes or less) 3) Portable 4) If test is performed at point of care, high likelihood that person will receive test result	1) Less sensitive for early infections than flow-through rapid tests, and IgM/IgG or p24 Antigen/IgM/IgG sensitive laboratory tests 2) Unigold, uses an IgM/IgG sensitive format but it was reported by CDC to have sensitivity similar to that of IgG sensitive tests with stored plasma

### IgG antibody sensitive flow-through rapid HIV immunoassays<sup>+++</sup>

<b>MedMira Reveal G3 Rapid HIV-1 Antibody Test</b>  <i>CLIA-moderate complexity</i>	<ol style="list-style-type: none"> <li>1) More sensitive during early infection than IgG sensitive lateral flow rapid HIV antibody tests <sup>**</sup></li> <li>2) Quick turnaround time (&lt; 5 minutes)</li> <li>3) Test can be read immediately after adding reagents.</li> <li>4) Portable</li> <li>5) If test is performed at point of care, high likelihood that person will receive test result</li> </ol>	<ol style="list-style-type: none"> <li>1) MedMira Reveal G3 Rapid HIV-1 Antibody Test is for use only with serum or plasma</li> <li>2) Less sensitive than IgM/IgG and p24 Ag/IgM/IgG sensitive tests</li> <li>3) FDA-approved for HIV-1 only</li> </ol>
<b>Multispot HIV-1/HIV-2</b>  <i>CLIA-moderate complexity differentiation test</i>	<ol style="list-style-type: none"> <li>1) More sensitive during early infection than lateral flow rapid HIV antibody tests</li> <li>2) Differentiates HIV-1 from HIV-2</li> <li>3) Quick turnaround time (&lt; 20 minutes)</li> <li>4) If test is performed at point of care, high likelihood that person will receive test result</li> <li>5) Test can be used either as a screening test or supplemental test in a diagnostic algorithm</li> </ol>	<ol style="list-style-type: none"> <li>1) For use only with serum or plasma</li> <li>2) Less sensitive for early HIV infection than IgM/IgG or p24 Ag/IgM/IgG sensitive tests</li> <li>3) If delivery of test result is delayed there is an increased likelihood person tested may not receive results</li> </ol>

### IgG antibody sensitive lateral-flow rapid HIV immunoassays<sup>\*\*\*</sup>

<b>Clearview HIV 1/2 STAT-PAK</b>  <b>Clearview COMPLETE HIV 1/2</b>  <b>OraQuick ADVANCE Rapid HIV-1/2 Antibody Test</b>  <i>All tests are CLIA-Waived when used with whole blood.</i>	<ol style="list-style-type: none"> <li>1) CLIA-waived tests can be performed by non-laboratorians</li> <li>2) Quick turnaround time (20 minutes or less)</li> <li>3) Portable</li> <li>4) If test is performed at point of care, high likelihood that person will receive test result</li> </ol>	<ol style="list-style-type: none"> <li>1) Less sensitive for early infections than flow-through rapid tests, and IgM/IgG or p24 Ag/IgM/IgG sensitive tests</li> <li>2) Rapid tests used with oral fluid, which has lower antibody concentration, are less sensitive and specific than when used with blood<sup>2,3,4</sup></li> </ol>
---	--	---

### IgG antibody sensitive dual-path platform HIV-1/HIV-2 immunoassay<sup>&\*\*\*</sup>

<b>Chembio DPP HIV-1/2</b>  <i>CLIA-waived when used with whole blood or oral fluid</i>	<ol style="list-style-type: none"> <li>1) Quick turnaround time (&lt; 20 minutes)</li> <li>2) If test performed onsite, high likelihood that person will receive test result</li> <li>3) Portable</li> <li>4) Can use venous or finger stick blood, oral fluid, plasma or serum</li> </ol>	<ol style="list-style-type: none"> <li>1) Less sensitive than IgM/IgG and p24 Ag/IgM/IgG sensitive tests</li> <li>2) Rapid tests used with oral fluid, which has lower antibody concentration, are less sensitive and specific than when used with blood<sup>2,3,4</sup></li> </ol>
---	--	---

## IgG antibody sensitive laboratory-based HIV-1 antibody immunoassay\*\*

<b>Avioq HIV-1 Microelisa System</b>  <i>Manual CLIA high complexity</i>	<ol style="list-style-type: none"> <li>1) Can be used with dried blood spots or oral fluid collected with the OraSure oral fluid collection device</li> <li>2) Low cost</li> </ol>	<ol style="list-style-type: none"> <li>1) Less sensitive for early infections than IgM/IgG or p24 Ag/IgM/IgG sensitive tests</li> <li>2) Results from specimens collected with the OraSure collection device have reduced sensitivity and specificity compared with blood specimens<sup>5</sup></li> <li>3) Labor intensive</li> <li>4) Long turnaround time (&gt; 3 hours); if delivery of test result is delayed there is an increased likelihood person tested may not receive results</li> <li>5) FDA-approved for HIV-1 only</li> </ol>
--	--	--

+ Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) tests are categorized by the complexity of the test. The more procedural steps and requirements for user interpretation, the more restrictions are placed on who can perform the test. CLIA-waived tests are simple laboratory tests where the likelihood of erroneous test results is negligible.

^For more information about using HIV tests in multi-test algorithms see "Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations" at <http://stacks.cdc.gov/view/cdc/23447> and a companion quick reference guide is available at <http://stacks.cdc.gov/view/cdc/23563>.

\*p24 Antigen/IgM and IgG antibody IAs use synthetic peptides and recombinant protein antigens allowing for detection of IgM and IgG antibodies in the direct IA format (antigen sandwich). A direct IA (antibody sandwich) component for detecting viral p24 antigen is also incorporated. The p24 antigen/IgM/IgG IA format maximizes specificity by using recombinant protein and peptide antigens for detection of HIV antibody and maximizes sensitivity by using increased sample volumes, allowing detection of IgM, IgG antibodies and viral p24 protein which is known to be present in blood prior to detectable HIV antibodies.

# Lateral flow rapid tests: the sample is placed in a sample area followed by a buffer which assists the sample in migrating across the strip in which all of the reactants and detectors are embedded.

~ IgM/IgG antibody sensitive IAs are constructed in the direct IA format (antigen sandwich) which allows for detection of IgG and IgM antibodies (generally made early after infection). Sensitivity is increased by allowing for the detection of IgM (first class of immunoglobulin made after infection) in addition to IgG and by increased sample volume input.

++ Flow-through rapid tests: Specimen, buffer and wash solution flow through a porous membrane in which the antigens are embedded and then onto an absorbent pad. A second layer inhibits the backflow of fluids, which can obscure results. Once the test is started, attention is required until the addition of the final wash buffer, but after that is added; the test can be read immediately.

\*\*IgG antibody sensitive IAs use synthetic peptides or recombinant protein antigens and detect IgG in an indirect IA format. The use of synthetic peptides and recombinant protein antigens improve specificity by eliminating cellular proteins that are contained in viral particles, and thus increase assay specificity by avoiding detection of antibodies to cellular proteins.

& Employs dual path lateral flow platform technology which consists of a sample path and reagent path that intersect in the antibody test and control areas in the read out window of the test cassette.

## References

1. Mashgadadi N, Galli R, Daly C, et al. Sensitivity of a rapid point of care assay for early HIV antibody detection is enhanced by its ability to detect HIV gp41 IgM antibodies. *Journal of Clinical Virology* October 2015, Vol. 71, p. 67-72. Doi:10.1016/j.jcv.2015.08.005
2. Mortimer PP and Parry JV. Non-invasive virological diagnosis: are saliva and urine specimens adequate substitutes for blood? *Reviews in Medical Virology* 1991; 1:73-78.
3. Pant Pai N, Joshi R, Dogra S, Taksande B, Kalantri S, et al. Evaluation of diagnostic accuracy, feasibility and client preference for rapid oral fluid-based diagnosis of HIV infection in rural India. *PLoS ONE* 2007; 2(4):e367. doi:10.1371/journal.pone.0000367
4. CDC. False-Positive Oral Fluid Rapid HIV Tests --- New York City, 2005—2008. *MMWR* 2008 / 57 (Early Release);1-5.
5. Avioq, Inc. Avioq HIV-1 Microelisa System [Package Insert]. Rockville, MD: Avioq, Inc. August, 2009.